Remarks

Applicant appreciates the thorough examination of the present application as evidenced by the Office Action dated July 16, 2007 (hereinafter, the "Office Action."). Claims 23, 26-35 and 45-83 are pending in the present application, and these claims stand rejected. More specifically, Claims 23, 26-35 and 45-83 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Dobbie, "Separation of Peritoneal Surfaces Through the Maintenance of an Artificial Ascites as a Preventative of Peritoneal Adhesions." Abstract, 4th Peritoneum and Peritoneal Access Meeting, September 16-19, 1997 (hereinafter, "Dobbie") in view of U.S. Patent No. 4,886,789 to Milner (hereinafter, "Milner") or Treutner et al. "Prevention of Postoperative Adhesions by Single Intraperitoneal Medication," *Journal of Surgical Research* **59**: 764-771 (1995) (hereinafter, "Treutner et al.). *See* Office Action, page 3.

The Office Action asserts that the factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966) in determining obviousness are summarized as follows:

1. Determining the scope and content of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Applicant respectfully submits that Claims 23, 26-35 and 45-83 set forth a patentable invention under the factors enumerated in *Graham v. John Deere* (for which factors 1, 2 and 4 will be discussed below) and under the guiding principles pronounced in *KSR International Co. v. Teleflex Inc., et al.* 550 U.S. 1, 12 (2007).

Determining the scope and content of the prior art.

The Office Action asserts that Dobbie "discloses development of Icodextrin (glucose polymer) as a non-glycating, long-dwell, peritoneal solution of physiological osmolarity for use in peritoneal dialysis as a dialysate, a carrier solution for continuous ambulatory chemotherapy, and for use post-operatively in patients with a high risk of abdominal adhesions." Office Action, page 3. The Office Action alleges that this statement "embraces the general description of the instantly claimed method of reducing the incidence of adhesions in a body cavity since the terms Icodextrin and non-glycating; peritoneal &

abdominal; post-operatively; and long-dwell all suggest the dextrin, body cavity, unsubstituted dextrin, post-operative and the period of time disclosed in the instant claims." Office Action, page 3.

Applicant submits that Dobbie fails to teach or suggest a method of reducing the incidence of post-operative adhesions as recited in the pending claims. The mere mention of the terms "Icodextrin," "non-glycating," "peritoneal," "abdominal," "post-operatively" and "long-dwell" do not teach or suggest the present invention recited in the pending claims. Applicant specifically notes that in the context of Dobbie and as is known to one of ordinary skill in the art, "long-dwell" refers to the longer of the four (4) times daily individual dialysis fluid dwells that a typical peritoneal dialysis patient is exposed to within a single 24 hour period. *See* Item 5 and Tab 2 of the previously submitted Declaration Under 37 C.F.R. §1.132 of Dr. Elizabeth Peers, MA. PhD (hereinafter, the "Peers Declaration").

Applicant respectfully submits that only through hindsight reconstruction using the present application as a guide is one of ordinary skill in the art provided with the direction to use said terms to formulate the present invention with the required degree of specificity in order to achieve the desired result. Dobbie merely states that the International Peritoneal Biopsy Registry (IPBR) advocates the use of glucose polymer (Icodextrin) for use post-operatively in patients with a high risk of abdominal adhesions. *See* Dobbie. This mere statement does not lead one of ordinary skill in the art to the following methods as recited in the independent claims of the present application:

Claim 23

> A method of reducing the incidence of post-operative adhesions in a body cavity, comprising introducing into the body cavity a composition comprising an aqueous formulation further comprising a polysaccharide dextrin in an amount effective to reduce the incidence of said post-operative adhesions, wherein the dextrin is unsubstituted and the dextrin contains more than 15% of polymers with a degree of polymerization (DP) greater than 12 and acts as an osmotic agent to ***maintain a volume of the aqueous formulation in the body cavity*** serving to separate tissues which otherwise may adhere to each other, and wherein the ***aqueous formulation is a solution in the body cavity*** and ***remains in the body cavity for at least 2 days***.

Claim 51

A method of reducing the incidence of post-operative adhesions in a body cavity, comprising introducing into the body cavity a composition comprising an aqueous formulation further comprising a polysaccharide dextrin in an amount effective to reduce the incidence of said post-operative adhesions, wherein the dextrin is unsubstituted and the dextrin contains more than 15% of polymers with a degree of polymerization (DP) greater than 12 and acts as an osmotic agent to ***maintain a volume of the aqueous formulation in the body cavity*** serving to separate tissues which otherwise may adhere to each other, and wherein:

(a) the ***aqueous formulation is a solution in the body cavity, remains in the body cavity for at least 2 days*** and is ***not removed***;

(b) the dextrin is applied to the body cavity in an amount of ***about 4 % weight to volume of the composition***; and

(c) the composition is ***administered intraperitoneally***.

Claim 57

A method of reducing the incidence of post-operative adhesions in a body cavity, comprising:

(a) introducing into the body cavity a composition comprising an aqueous formulation further comprising a polysaccharide dextrin in an amount effective to reduce the incidence of said post-operative adhesions, wherein the dextrin is unsubstituted and the dextrin contains more than 15% of polymers with a degree of polymerization (DP) greater than 12 and acts as an osmotic agent to ***maintain a volume of the aqueous formulation in the body cavity*** serving to separate tissues which otherwise may adhere to each other, and wherein the ***aqueous formulation is a solution in the body cavity***; and

(b) allowing the aqueous formulation to ***remain in the body cavity for at least 2 days***, wherein the aqueous formulation is ***not removed from the body cavity***.

Claim 67

A method of reducing the incidence of post-operative adhesions in a body cavity, comprising introducing into the body cavity a composition comprising an aqueous formulation further comprising a polysaccharide dextrin in an amount effective to reduce the incidence of said post-operative adhesions, wherein the dextrin is unsubstituted and the dextrin contains more than 15% of polymers with a degree of polymerization (DP) greater than 12 and acts as an osmotic agent to ***maintain a volume of the aqueous formulation in the body cavity*** serving to separate tissues which otherwise may adhere to each other, and wherein the aqueous formulation is a solution in the body cavity ***administered under surgical conditions*** and the aqueous formulation ***remains in the body cavity*** and is ***not removed***.

Claim 77

> A method of reducing the incidence of post-operative adhesions in a body cavity, comprising introducing into the body cavity a composition ***comprising less than 2000 ml of an aqueous formulation*** further comprising a polysaccharide dextrin in an amount effective to reduce the incidence of said post-operative adhesions, wherein the dextrin is unsubstituted and the dextrin contains more than 15% of polymers with a degree of polymerization (DP) greater than 12 and acts as an osmotic agent to ***maintain a volume of the aqueous formulation in the body cavity*** serving to separate tissues which otherwise may adhere to each other, and wherein the ***aqueous formulation is a solution in the body cavity*** and the aqueous formulation ***remains in the body cavity*** and is ***not removed***.

Purportedly, any deficiencies in Dobbie are cured by the cited secondary references. However, Milner discusses a peritioneal dialysis solution that is simply not applicable for at least the reasons previously made of record and as further discussed below. Applicant respectfully submits that the newly cited Treutner et al. reference also fails to cure the deficiencies of Dobbie. As noted in the Office Action, Treutner et al. discusses the administration of various types of products post-operatively in a single application (see Office Action, page 4); however, none of the nine different substances is a dextrin composition or such that a dextrin composition is suggested by the use of these substances listed in Treutner et al. In summarizing the research, Treutner et al. states, "Our data indicate that lipid compounds, as well as hyaluronic acid and TCDO [tetrachlorodecaoxide], are the most likely candidates to fulfill the requirements for a routine clinical application [to prevent postoperative adhesions]." Treutner et al., page 770, second column, ¶3. These substances are not the same or similar to dextrin. Furthermore, these substances do not direct one of ordinary skill in the art to a dextrin composition or to a method of its use. Dextrin is a glucose polymer and the substances advocated as "likely candidates" in Treutner et al are polar lipid compounds, a naturally-occuring glycosaminoglycan composed of D-glucuronic acid and D-N-acetylglucosamine units linked together via alternating β-1,4 and β-1,3 glycosidic bonds, and an anion complex containing oxygen in a chlorite matrix, respectively.

The Office Action asserts that "the [Treutner et al.] products remain for an extended period of time as disclosed in instant claims 23, 27, 29, 45, 62, 72 and 81" (Office Action, page 4) and further asserts that "[t]he amount of substances used in the Treutner reference (a volume of 1 ml per 100 g body wt.) embraces the amount of the composition used in instant

Claims 30, 31, 63, 64, 73 and 74" (Office Action, page 4). Applicant respectfully disagrees and submits that it is merely a presumption that the products used by Treutner et al. remain for an extended period of time as recited in the pending claims as there is **no** discussion or suggestion in Treutner et al. regarding the period of time for which the products remained in the body cavity. Regarding the amount of substance used in Treutner et al., at a volume of 1 ml per 100 g body weight, this amount does not embrace the volume range of 1000-1500 ml recited in Claims 31, 64 and 74. However, Applicant again notes that the substances employed in Treutner et al. are neither dextrin compositions nor similar to dextrin compositions. Thus, Applicant asserts that the volume cited in Treutner et al. is not relevant to the present methods recited in Claims 30, 31, 63, 64, 73 and 74.

Clearly, the scope and content of the cited references, alone or in combination, do not provide sufficient description to teach or suggest the present invention. The deficiencies are impermissibly supplied by the Applicant's disclosure.

Ascertaining the differences between the prior art and the claims at issue.

In addition to the deficient scope and content of the cited references with respect to the present invention, there are fundamental differences between the disclosure of the cited references and the present invention that fail to lead one of ordinary skill in the art toward the present invention. Moreover, some of the differences teach one of ordinary skill in the art away from the present invention.

As noted above, Dobbie merely presents a statement regarding a general proposal to use glucose polymer (Icodextrin) for use post-operatively in patients with a high risk of abdominal adhesions. Without more, one of ordinary skill in the art is not directed to methods of reducing post-operative adhesions as recited in the pending claims.

Milner, which is directed to peritoneal dialysis, does not provide the additional disclosure that is needed to arrive at the present invention. As noted in the Peers Declaration, there are clear fundamental distinctions between ***peritoneal dialysis*** and ***methods of adhesion reduction*** as disclosed in the present application. For example, peritoneal dialysis involves, among other things: (a) continuous flux of fluids in and out of the peritoneal cavity, (b) each "dwell" of dialysis fluid draws into the peritoneal cavity waste products and excess fluid from the patient's circulation, (c) "dirty" fluid is drained out and replaced with clean fluid at each "exchange," thereby forming the next dwell period and (d) peritoneal dialysis is a patient-

managed, daily, chronic and/or long-term treatment. In contrast, the methods of adhesion reduction described in the present application are, among other things: (a) neither a daily nor long-term treatment, (b) administered by a healthcare professional, typically in an operating room or other medical setting, and (c) serving to maintain a volume of the aqueous solution. Further, there are medical reasons not to use a peritoneal dialysis solution for adhesion reduction that can include the potential of abdominal bulging, risk of infection when the fluid is not drained, and risk of dehydration as a result of the drawing-in of fluid into the peritoneal cavity from the circulation. Medical reasons not to use an adhesion reduction solution in peritoneal dialysis can include the failure to draw in fluid and/or waste and the unsuitability of the smaller volume associated with the adhesion reduction solution. Thus, one of ordinary skill in the art would not consider Milner for its presumed teachings **absent viewing the present application first** in order to gain insight to the methods of using the composition in a method of reducing post-operative adhesions as claimed.

Again, Truetner et al. discusses possible substances for use to prevent post-operative adhesions. These possible substances do not suggest that one of ordinary skill in the art should use a peritoneal dialysis solution, or a solution including dextrin, in a method of reducing post-operative adhesions as claimed.

Accordingly, the differences between the cited references and the claims at issue establish that these references do not teach or suggest the present invention and the distinctions between peritoneal dialysis and the Applicant's peritoneal adhesion prevention technology actually teach one of ordinary skill in the art away from the present invention if relying upon the cited references and/or the knowledge and routine practice of one of ordinary skill in the art immediately prior to the filing date of the present application.

Considering objective evidence indicating obviousness or nonobviousness.

The Office Action indicates that a factual inquiry set forth in *Graham v. John Deere Co.*, includes considering objective evidence present in the application indicating obviousness or nonobviousness. *See* Office Action, page 3. Applicant has previously submitted objective indicia of nonobviousness consistent with the Manual of Patent Examining Procedure (MPEP) §716.01(a) noting that long-felt but unsolved need and commercial success are indicia of nonobviousness.

Applicant has more than sufficiently discussed the long-felt need for Applicant's invention in Applicant's previous response noting that adhesions are the single greatest complication of surgery (Young et al. *Fertility and Sterility* **84**: 1450-1456 (2005)) and further noting that 93% of patients undergoing abdominal surgery are affected by adhesions (Menzies and Ellis. *Annals Royal College of Surgeons of England* **72**:60-63 (1990)). This long-felt need is further noted by Treutner et al. now cited by the Examiner.

The long-felt need for a product to prevent post-operative adhesions has been met by Applicant's invention; aspects of which have been a commercial success as marketed by Baxter Healthcare Corporation as Adept®. Adept® is a clinically effective product shown to reduce the incidence of adhesions after gynecological laparoscopic surgery, and thus, Adept® presents a scientific advance in surgical procedures. Data in support of this statement as well as the package insert information for Adept® were previously submitted with the Peers Declaration. Further, and quite notably, Baxter licensed a dextrin ***peritoneal dialysis solution*** in 1996. Baxter has recognized the fundamental difference between the peritoneal dialysis solution and the adhesion reduction solution and is now a licensee of the ***adhesion reduction technology*** as claimed.

Thus, not only has Applicant shown that the Examiner has failed to establish a *prima facie* case of obviousness under 35 U.S.C. §103, but Applicant has further provided rebuttal evidence presenting objective indicia of nonobviousness.

In summary, a patent composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art. *KSR Int'l Co. v. Teleflex Inc.,* 550 U. S. 1, 15 (2007). A Court must ask whether the improvement is more than the predictable use of prior art elements according to their established functions. *Id.* at 13. When it is necessary for a Court to look at interrelated teachings of multiple patents, the Court must determine whether there was an apparent reason to combine the known elements ***in the fashion claimed by the patent at issue***. *Id.* at 14 (emphasis added). For at least the reasons previously made of record and those set forth above, it clear that the references either teach away from the present invention or one of ordinary skill in the art must use the Applicant's disclosure as a guide to employ the cited references in order to fashion the claimed invention. Applicant further submits objective indicia of nonobviousness of the present invention, which must also be considered in this analysis.

Accordingly, Applicants respectfully submit that Claims 23, 26-35 and 45-83 are not obvious in view of the cited references, and Applicant respectfully requests that this rejection be withdrawn.

Conclusion

In view of the foregoing remarks, Applicant respectfully requests that all outstanding rejections to the claims be withdrawn and that a Notice of Allowance be issued in due course.

The Examiner is invited and encouraged to contact the undersigned directly if such contact will expedite the prosecution of the pending claims to issue. In any event, any questions that the Examiner may have should be directed to the undersigned, who may be reached at (919) 854-1400.

Respectfully submitted,

Shawna Cannon Lemon
Registration No. 53,888

USPTO Customer No. 20792
Myers Bigel Sibley & Sajovec, P.A.
P. O. Box 37428
Raleigh, North Carolina 27627
Telephone: (919) 854-1400
Facsimile: (919) 854-1401

CERTIFICATION OF TRANSMISSION

I hereby certify that this correspondence is being transmitted via the Office electronic filing system in accordance with § 1.6(a)(4) to the U.S. Patent and Trademark Office on December 11, 2007.

Laneisha C. Hayes
Date of Signature: December 11, 2007